High-Altitude Pulmonary Edema in Vail, Colorado, 1975-1982

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Between 1975 and 1982 a total of 47 cases of high-altitude pulmonary edema occurred in Vail, Colorado, elevation 2,500 m (8,200 ft). All occurred in visitors from lower altitudes. The mean age of the patients was 35.6 years, and 93% were men. Most patients had tachycardia, tachypnea and fever. The mean time of onset of cough and shortness of breath was 2.5 days after arrival. The average total ascent of the patients was 2,330 m (7,644 ft) in less than one day from a mean residential elevation of 170 m (556 ft). Also, 91% of the cases occurred between December and April, when the average daily temperature was −4.3°C (24.3°F) and the ambient barometric pressure was 22.37 in of mercury.

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In a previous study of high-altitude pulmonary edema (HAPE) among visitors to Summit County, Colorado, it was suggested that there are two epidemiologically distinct varieties of the disease.[1] Type I (nonresident-ascent) HAPE was seen to affect residents of altitudes below 2,438 m (8,000 ft) who ascend to higher altitudes for periods of two days or longer. The patients in whom this disorder develops are men with a mean age in the mid-30s.

In contrast, type II (resident-reascent) HAPE affects residents of high altitudes after they return from descents to elevations below 2,438 m. This variety of HAPE appears to be a disorder primarily of childhood and adolescence, with a mean age of 9 to 12 years, and affects males and females equally.

In this study I analyze all cases of HAPE that were seen in Vail, Colorado (base elevation 2,500 m [8,200 ft]), between 1975 and 1982. The objectives of this report are threefold: to describe the clinical and epidemiologic characteristics of the disorder found at this elevation, to look closely at unusual cases for clues to the causes of the disorder and to examine the hypothesis that there are two distinct epidemiologic varieties of HAPE.

Methods

HAPE Patients

The hospital or outpatient records of all patients with HAPE who were examined radiographically at the Vail Hospital (46 patients representing 47 cases of HAPE) between 1975 and 1982 were collected. They were analyzed with respect to the patient's age, sex, vital signs and laboratory results, altitude of residence, time until onset of symptoms, disposition and outcome.

The diagnosis of high-altitude pulmonary edema was based on a medical history of cough developing within 72 hours (with only one exception) of arrival at altitude and a physical examination with findings of rales and cough with deep inspiration. In all cases the diagnosis was confirmed radiologically on finding the characteristic fluffy, usually asymmetric infiltrate with a normal cardiac silhouette on posteroanterior and lateral chest films (Figure 1). Outcome was assessed both clinically and radiologically by the attending physicians.

Patients seen in outpatient facilities who were diagnosed as having possible HAPE were sent to the hospital's radiology department, which has the town's only radiologic equipment. There Gerald Dooher, MD, maintains an index of HAPE cases to facilitate studies such as this one.

Once the diagnosis was confirmed, the patient was either admitted to the Vail Hospital (38 of 46 patients), treated on an outpatient basis in Vail or sent to Denver.

Controls

The medical records of 100 patients from out of state were selected randomly from Vail Mountain Medical Center's outpatient clinic records. These patients did not have HAPE but did have other medical problems requiring attention at the Vail physicians' office. Charts for persons from out of state were selected because these patients matched certain characteristics of the HAPE patient population: they invariably re-

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ABBREVIATIONS USED IN TEXT
ADH = antidiuretic hormone
HAPE = high-altitude pulmonary edema

sided at altitudes below 2,438 m (8,000 ft) and spent more than two days in Vail. These records were analyzed for patients' ages and sex.

Statistical Analysis

Normal Z values were used for all tests of significance.

Vail and Its Hospital

In 1980 the town of Vail, a mountain resort community, had 2,261 year-round inhabitants.[2] It lies within Eagle County, population 13,320. Elevations in the Vail Valley range from 2,438 to 3,962 m (8,000 to 13,000 ft). Both visitors and residents spend most of their waking and sleeping hours between 2,438 and 2,743 m (8,000 and 9,000 ft). Skiers at Vail routinely ascend to 3,048 m (10,000 ft) at Mid-Vail, and many go to the top of the mountain above 3,353 m (11,000 ft) for short periods before skiing down to Mid-Vail.

The Vail Valley Medical Center serves the medical needs of virtually all of Eagle County's residents and visitors. Patients are seen in the hospital's emergency room, in the Vail Mountain Medical Family Practice Office or in other private practices. At the time of this study, there was no pediatrician in Vail, nor were there separate radiologic facilities in any physician's office.

Climatologic data consisting of daily high and low temperatures for the winter months from January 1980 through April 1982 were provided by the Vail Nature Center. The day each case presented was identified, and the weather data for the preceding 72 hours were analyzed. Frank Doll, a resident of Avon, Colorado, provided both barometric pressures (normalized to sea level) and prevailing weather conditions for those dates. These pressures were reduced by 7.6 in of mercury because the unadjusted ambient barometric pressure at 2,500 m (8,200 ft) is 22.4 in of mercury.[3]

Because male visitors who lived at altitudes of 1,524 m (5,000 ft) or lower and stayed in Vail longer than two days were seen to be at risk for the development of HAPE at Vail's elevation, the prevalence of the disorder for this group was calculated. Vail Associates, the company managing the Vail Ski Area, calculated the total number of tickets sold for the years 1980, 1981 and 1982 and provided demographic characteristics of Vail skiers.

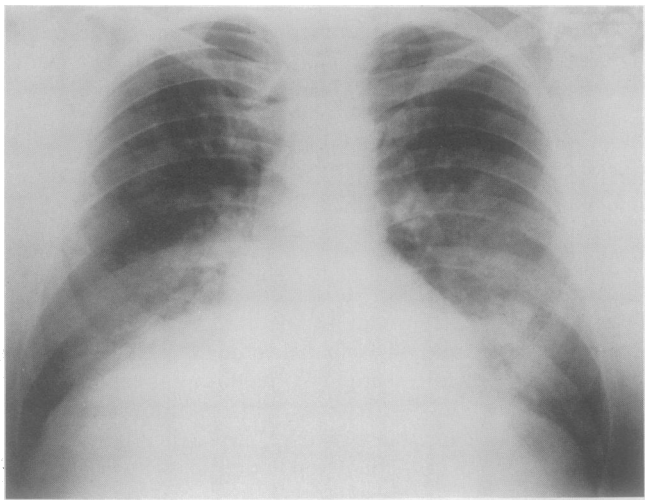

Figure 1.—Radiographic appearance of the chest in cases of high-altitude pulmonary edema at 2,500 m (8,200 ft).

Results

Mean Age of HAPE Patients and Controls

A total of 46 patients were diagnosed as having 47 cases of HAPE between January 1975 and December 1982. In one patient the disorder first developed in 1976 and then again in 1982. This was the only recurrence among the 46 patients. The mean age of this group was 35.6 years with a standard deviation of 10.2 years. The range of ages was 12 to 55 years.

The mean age of the control population was 32.9 years with a standard deviation of 16.8 years and a range of 0.5 to 63 years. The mean ages of HAPE and control groups differed significantly at $P < .05$.

Sex Distribution of HAPE Patients and Controls

There were 43 male HAPE patients (93%) and 3 (7%) female. In the control population, 45% were male and 55% female. The male-to-female ratios of these two groups differed significantly at $P < .001$.

Unusual cases. High-altitude sickness developed in only three women in Vail between 1975 and 1982. One was a 55-year-old woman from Brooklyn, New York, who was presumably postmenopausal. Another was a 33-year-old woman from Brookline, Massachusetts, with a possible infertility problem ever since her one pregnancy spontaneously aborted. The third was a 30-year-old woman from Fort Wayne, Indiana, who was being treated for hypothyroidism and had been told by her physician that she had a possible pituitary problem.

Vital Signs and Laboratory Data

Tachycardia, tachypnea and elevation of body temperature characterized the Vail patients who had HAPE. As seen in Table 1, heart rates ranged from 76 to 160 per minute (mean 111), respiratory rates from 12 to 55 per minute (mean 26) and body temperatures taken orally from 36.9°C to 39°C (98.4°F to 102.4°F [mean 99.8°F]).

TABLE 1.—*Vital Signs of Vail HAPE Patients*

Heart rate/min (20 patients)	
Range	76-160
Mean	111
Blood pressure, mm Hg (24 patients)	
Systolic	
Range	98-170
Mean	140
Diastolic	
Range	70-129
Mean	89
Respiratory rate/min (16 patients)	
Range	12-55
Mean	26
Body temperature, °C (°F) (18 patients)	
Range	36.9-39 (98.4-102.4)
Mean	37.7 (99.8)

HAPE = high-altitude pulmonary edema

The laboratory findings for the Vail cases of HAPE are summarized in Table 2. Leukocyte counts were elevated with a left shift. Though some patients produced concentrated urine, the mean specific gravity was 1.017. The time of collection was not specified on patient charts, so even though the results of only urinalyses dated on the day of admission were reported above, it is possible that results do not accurately reflect urine specific gravities before treatment. Arterial oxygen concentration was notably below normal in the five severely ill patients who underwent arterial blood gas testing, but arterial carbon dioxide pressures were normal.

Onset of Symptoms

Data were available for 32 of 47 cases. The mean time of onset of cough and shortness of breath was 2.5 days with a standard deviation of 0.8 days. The range was one to five days.

Unusual case. The patient, a 39-year-old male dwarf, came to Vail from Connecticut in March 1976. A cough productive of frothy, blood-tinged sputum developed 24 hours after he arrived at altitude. On physical examination he had diffuse rales in both lungs, a pulse of 150 per minute, a blood pressure of 160/92 mm of mercury, a temperature of 37°C (98.6°F) and a respiratory rate of 20 per minute. His lips and nail beds were cyanotic. A chest x-ray film showed an increased transverse cardiac diameter related to the patient's dwarfism and patchy infiltrates in both lungs. He was admitted to hospital and treated with oxygen, bed rest and given furosemide (Lasix) by mouth and morphine sulfate intramuscularly. Clinical and radiologic improvement was noted in one day. Complete improvement radiologically occurred by day 3, and on day 4 the patient was discharged in good condition.

Treatment and Outcome

Data were available for 32 of 47 cases. All patients admitted to Vail Hospital were given oxygen by mask or nasal canula at a rate of 4 to 8 liters per minute. Of the 32 patients, 20 were treated with oral or intravenous administration of furosemide. Those treated with this drug had a mean hospital stay of two days (standard deviation of 0.8 days). The 12 patients not given furosemide or any other diuretic had a mean hospital stay of 1.6 days (standard deviation of 0.8 days).

Unusual case. The patient, a 28-year-old man, came to Vail from Morristown, New Jersey, in February 1976. Two and a half years before this visit, diabetes insipidus of unknown cause had developed, for which he was treated with vasopressin nasal spray (Diapit). He used two or three sprays in each nostril four or five times a day and remembered taking more after arrival at altitude because he felt he was producing more urine than usual. Before the onset of this disease, he had visited high altitudes many times without having HAPE develop. Since the development of diabetes insipidus, however, he had had HAPE twice: the first time in Alta, Utah, in 1975 and the second time three days after his arrival in Vail in 1976. On physical examination at the time of his admission to Vail Hospital, he had rales in both lungs. His chest x-ray film showed infiltrates bilaterally, the right side worse than the left. He was treated with oxygen and bed rest, and his vasopressin spray therapy was withheld. Diuresis resulted, and the HAPE resolved in two days at which time he was again started on the use of vasopressin nasal spray.

Average Distance of Ascent and Altitude of Origin

Data were available for 42 of 47 cases. The mean altitude of origin was 170 m (556 ft) above sea level, with a standard deviation of 254 m (832 ft). The range was 0 to 1,524 m (5,000 ft). The average total ascent was 2,330 m (7,644 ft), with a range of 975 to 2,500 m (3,200 to 8,200 ft). Typically, this ascent is made by airplane and automobile or bus in less than 12 hours.[4]

Unusual case. The patient, a 34-year-old male physician, came to Vail in January 1982 from his home in the southern Arizona mountains, elevation 1,524 m (5,000 ft). After flying to Denver and then driving to Vail, he arrived at 2,500 m (8,200 ft) six hours after departing from home. He then played racquetball, slept and was on the slopes skiing the next day. The patient, a nonsmoker, had not exercised during the preceding year. His symptoms began on his third day in Vail, after two days of vigorous skiing. During the third night, he coughed up white, frothy sputum and became short of breath. He was admitted to hospital and recovered uneventfully. In 1982 he returned to Vail using acetazolamide (Diamox) to prevent HAPE and was less active after arrival. HAPE did not recur.

Month of Onset and Climatologic Conditions

As Table 3 shows, 43 of the 47 HAPE cases (91%) occurred between December and April. Only three cases occurred in July or August. There were 22 cases seen during the months for which climatologic data were available. The

TABLE 2.—*Laboratory Data From Vail HAPE Patients*

Hematocrit, % (28 patients)	
Range, 37-53	
Mean, 45.6	
Leukocyte count/μl (31 patients)	
Range, 6,800-20,800	
Mean, 11,496	
Segmented leukocyte count, % (25 patients)	
Range, 46-88	
Mean, 74	
Urine specific gravity (21 patients)	
Range, 1.005-1.035	
Mean, 1.017	
Arterial oxygen pressure, torr (5 patients)	
Range, 18-40	
Mean, 29.4	
Arterial carbon dioxide pressure, torr (5 patients)	
Range, 23-36	
Mean, 29.6	

HAPE = high-altitude pulmonary edema

TABLE 3.—*Month of Occurrence of 47 Vail HAPE Cases*

Month	Number of Cases	Month	Number of Cases
January	8	July	2
February	11	August	1
March	11	September	0
April	5	October	1
May	0	November	0
June	0	December	8

HAPE = high-altitude pulmonary edema

TABLE 4.—*The Prevalence of Type I HAPE Among Male Visitors to Vail*

Year	Number of Lift Tickets Sold	Number of Males at Risk	Prevalence HAPE Cases	Prevalence Cases/ 100,000
1979-1980	1,219,178	102,248	10	9.8
1980-1981	1,040,819	71,736	10	13.9
1981-1982	1,344,167	94,888	6	6.3
Totals	3,604,164	268,872	26	10.0

HAPE = high-altitude pulmonary edema

average daily temperature during the 72 hours preceding the diagnosis of HAPE was −4.3°C (24.3°F) with a standard deviation of −13.7°C (7.3°F). The range of average daily temperatures was −12.5°C (9.5°F) to 2.1°C (35.8°F). Eleven pre-HAPE periods (72 hours) were stormy, and ten were clear. The average daily ambient barometric pressures during pre-HAPE periods was 22.37 in of mercury with a standard deviation of 0.18. The range of daily barometric pressures was 21.99 to 22.76 in of mercury.

HAPE Prevalence Among Visitors to and Residents of Vail

Vail Associates marketing studies indicated that 69% to 74% of Vail and Beaver Creek ski tickets were sold to men and 50% to 68% were sold to out-of-state "destination" skiers who spent more than two days in Vail. Additionally, destination skiers spent an average of seven days in Vail and skied an average of six days while there. The typical out-of-state male skier came to Vail with his wife and 1.5 children.

Table 4 presents annual lift ticket sales, estimated number of men at risk for type I HAPE developing and the estimated prevalence of the disorder for the years 1980 through 1982. The average prevalence for that three-year period was 10 cases per 100,000 male visitors from elevations below 2,438 m (8,000 ft). There were only two cases among the estimated 268,872 female visitors between 1979 and 1982, yielding a prevalence of 0.74 per 100,000 females.

There were no cases of type II (resident-reascent) HAPE among Vail residents from 1975 through 1982.

Discussion

Clinical and Epidemiologic Characteristics of Type I HAPE at 2,500 M (8,200 Ft)

All of the Vail patients with HAPE were visitors to Vail rather than residents. Of 46 in this study, 43 (93%) were men, whereas Vail Associates marketing data and analysis of the out-of-state control group indicate that the population of out-of-state visitors consists of equal numbers of men and women. This finding is similar to that of a previous study of visitors to Summit County, Colorado (base elevation 2,743 to 3,048 m [9,000 to 10,000 ft]), in which all the HAPE patients were male.[1] The mean age of the Vail HAPE patients is also in the mid-30s, as was the Summit County group's.

The Vail patients with HAPE had tachycardia, tachypnea and fever. The onset of symptoms occurred an average of 2.5 days after arrival (range 1 to 5 days). Both the symptoms and time until onset were similar to those described at higher altitudes in the Himalayas[5,6] and in the Andes.[7-9] Of 32 cases, 12 (37%) improved on oxygen and bed rest, as did patients in Peru at 3,750 m (12,300 ft).[9]

The average total ascent of the HAPE patients was 2,330 m (7,644 ft) in less than 12 hours from an average residential elevation of 170 m (556 ft). For HAPE to develop at 2,500 m (8,200 ft), a rapid ascent of more than 2,330 m (7,600 ft) is usually required. Menon, on the other hand, reported that between 3,353 and 5,486 m (11,000 and 18,000 ft), a change of as little as 305 m (1,000 ft) could precipitate pulmonary edema.[5] Thus, at higher altitudes a shorter ascent will cause the disorder, and, conversely, at lower altitudes a greater change in elevation is required.

The seasonality noted among Vail HAPE cases probably reflects, at least in part, the fact that most visitors come to Vail during the winter months. The months of December through April are also the coldest months of the year when winter storms cause low temperatures and fluctuating barometric pressures. Thus, the average daily temperature of −4.3°C (24.3°F) on days preceding HAPE occurrences supports the idea that cold or stormy weather predisposes to the development of the disorder.

The prevalence of type I HAPE among male visitors who spend more than two days at 2,500 m (8,200 ft) is 10 cases per 100,000. This is consistent with the estimate of 10 to 100 cases per 100,000 visitors to Summit County, Colorado,[10] and much lower than the prevalences reported at higher altitudes. Menon found the incidence of HAPE among men flown to 3,500 m (11,500 ft) to be 0.57% or 570 cases per 100,000 men at risk.[5] Among men flown to 4,420 m (14,500 ft), the incidence was 15.5%.[6] Thus, it appears that the prevalence of type I HAPE is a function of the altitude reached, with a low of 10 cases per 100,000 male visitors at 2,500 m (8,200 ft) to a high of 15,500 cases per 100,000 at 4,420 m (14,500 ft).

Etiologic Clues From Unusual Cases

HAPE developed in three women in Vail between 1975 and 1982. One was 55 years old and presumably postmenopausal, one was hypothyroid and one had a possible infertility problem. These cases suggest that premenopausal women with physiologic levels of female hormones are somehow protected from HAPE, at least in the low range of high altitudes.

The work of Wetzel and Sylvester suggests one explanation for this finding.[11,12] They have shown that hypoxia causes a greater vasoconstrictive response in male than in female isolated sheep lungs. The difference reflects an attenuation of the vasoconstrictive reaction in female sheep that is mediated by estradiol. Assuming that hypoxic vasoconstriction occurs in humans at the arteriolar or venular level, an assumption supported by the finding by Fasules and co-workers of increased lung vasoreactivity in children after recovery from HAPE,[13] a similar mechanism could account for the apparent protection women enjoy.

That HAPE developed in one patient after strenuous exertion following a relatively short ascent of 975 m (3,200 ft) suggests that the tendency for the disorder to develop is also a function of activity at altitude. Singh and associates[6] concluded that severe exertion predisposed men to pulmonary edema at 3,353 to 4,420 m (11,000 to 14,500 ft). They suggested that exertion aggravates hypoxia, which in turn causes pulmonary vasoconstriction. Similarly, Menon[5] reported that 35 of 101 cases in which HAPE developed at 3,500 m (11,500 ft) followed moderate to severe exertion (digging,

handling heavy equipment or lifting). Thus, strenuous exercise seems to be sufficient but not necessary to predispose to the development of HAPE.

That the disorder developed repeatedly in one patient after the onset of diabetes insipidus and treatment with exogenous vasopressin deserves attention. Failure to diurese because of too much vasopressin is a possible explanation of this patient's recurring susceptibility to HAPE. Whether oversecretion of vasopressin (antidiuretic hormone [ADH]) accounts for the occurrence of HAPE in other patients warrants consideration. Hackett and associates have shown elevated ADH levels in climbers with HAPE[14] and have observed that the symptoms of acute mountain sickness are worse in patients who fail to diurese, gain rather than lose weight and produce a highly concentrated urine during ascent to high altitudes.[15,16] The repeated occurrence of HAPE in a patient with diabetes insipidus treated with exogenous vasopressin lends causal significance to these observations.

The development of HAPE in a male dwarf within 24 hours of arrival should be noted even though etiologic clues are not evident. Whether short stature or an underlying endocrine disorder related to inadequate levels of growth hormone are risk factors is purely conjectural at this time.

The HAPE Model

As described in the introduction, two epidemiologically distinct types of HAPE have been described: type I (nonresident-ascent) HAPE, which affects residents of low altitudes when they visit high altitudes, and type II (resident-reascent) HAPE, which affects residents of high altitudes when they return from visits to lower altitudes. Type I affects predominantly men with a mean age in the mid-30s. Type II affects males and females equally. The mean age of this group is 9 to 12 years.

All HAPE cases at 2,500 m (8,200 ft) were type I, and type II HAPE was not found at this altitude. In addition, 93% of the Vail patients with HAPE were men, compared with only 45% of the control group. Because the disease developed in only three women in seven years, men appear to have at least a 13-fold greater risk for the disorder developing at these elevations. In contrast, predominantly type II HAPE groups studied in Leadville, Colorado,[17] and Peru[7-9] showed that male and female subjects were at approximately equal risk of having the disorder. Finally, the mean age of the Vail HAPE patients was 35.6 years, whereas the type II patients observed in Leadville, Colorado, and Peru had mean ages of 9 to 16 years. Thus, types I and II appear to be epidemiologically distinct in that they have differing threshold altitudes, affect males and females differently and affect different age groups.

In conclusion, the findings of the present study suggest that the tendency for type I HAPE to develop is a function of the rate and the distance of ascent, the altitude attained and the visitor's activity level after arrival. Men appear to be at much greater risk than healthy premenopausal women, perhaps because the latter group is protected from the disorder by a mechanism related to the presence of physiologic quantities of one or more female hormones. An etiologic role for the inappropriate secretion of antidiuretic hormone caused by hypoxia is possible. It is hoped that further definition of the epidemiologic model of HAPE will advance our understanding of this intriguing disorder.

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